

REMARKS

Pursuant to the entry of the instant amendment, claims 2, 4-15, 17, and 24 are presently pending. In an effort to expedite prosecution, Applicants have amended the sole independent claim – claim 2 – to incorporate the limitations of claim 9, now canceled. Thus, the claims as presently pending are directed to a process for the production of a composition containing at least one coagulation factor that consists of:

- i. adjusting the pH of a plasma fraction, wherein said plasma fraction contains an initial amount of fibronectin and at least one coagulation factor, contains NaCl or KCl at a concentration of 100 – 200 mM, and is characterized by an ionic strength below 500 mM to a value between pH 4.7 and pH 5.3 so as to form a precipitate comprising 70% to 99% of the initial amount of fibronectin and a supernatant containing said at least one coagulation factor,
- ii. removing the fibronectin precipitate formed in step (i) to thereby yield a composition containing at least one coagulation factor; and
- iii. treating the composition obtained in step (ii) to yield at least one purified coagulation factor,

wherein steps (i) and (ii) are performed at a temperature that ranges from 20°C to 25°C.

Applicants have further amended claim claims 2, 6, and 8 to address minor issues of clarity raised by the Examiner in the previous office action.

Support for the claims as amended is found in the specification as originally filed, particularly at page 4, lines 6-8 [“The concentration of sodium chloride or potassium chloride in the plasma fraction is preferably 50 to 250 mM, more preferably 100 to 200 mM, most preferably 120 to 150 mM.”]. Thus, Applicants respectfully submit that no new matter has been added. However, Applicants reiterate that these amendments are presented solely for the purpose of expediting prosecution and should not be construed as Applicants’ agreement with or acquiescence to the grounds of rejection previously set forth.

At present, all claims stand rejected on prior art grounds. However, Applicants submit that the prior art fails to disclose or suggest the process of the claims as amended herewith and respectfully petitions for reconsideration and withdrawal of the outstanding rejections in view of the amendments and remarks herein.

Turning now to the Office Action of September 2, 2009:

Minor Objections and Rejections

The Examiner objected to claim 8 for including an improper insertion of the word “is” at line 3. The amendment to claim 8 presented herewith corrects this matter.

The Examiner rejected claims 2, 4-15, 17, and 24 under 35 U.S.C. § 112, second paragraph, as being indefinite, noting that claim 2(i) failed to provide proper antecedent basis for the phrase “the plasma fraction”. The amendment to claim 2 presented herewith corrects this matter.

The Examiner suggested that the use of the open-ended term “comprises” in claim 6 is in conflict with the closed “consisting of” language of claim 2 and gives rise to the presumption that the “adjusting”, “removing”, and “treating” steps recited in claim 2 may encompass one or more sub-steps. To expedite prosecution, Applicants have amended claim 6 to include the noted closed language and accordingly submit that a reasonable interpretation of claim 2 requires the treatment of each recited process as a singular mono-step.

Thus, Applicants respectfully submit that the pending claims meet the threshold requirements of clarity and precision and respectfully petition for reconsideration and withdrawal of the outstanding rejections thereof.

Obviousness Rejections

Claims 2, 4-8, 14, and 24 stand rejected under 35 U.S.C. § 103(a) as being obvious in view of Wallace et al. (USPN 4,341,764, referred to hereinafter as “Wallace”). Claims 9-13 stand rejected under 35 U.S.C. § 103(a) as being obvious in view of Wallace in view of Newman (USPN 5,710,254, referred to hereinafter as “Newman”). Claims 15 and 17 stand rejected under 35 U.S.C. § 103(a) as being obvious in view of Wallace in view of Burnouf-Radosevich (USPN 5,408,039, referred to hereinafter as “BR”).

Applicants respectfully disagree, both with the Examiner’s characterization of the prior art teachings and with her conclusion of obviousness, and submit that the Examiner’s reliance on the Wallace reference in teaching or suggesting the bulk of the presently claimed process is misplaced. For example, the Examiner cites to Wallace’s recitation of a temperature range of 2° - 20° C and a pH of 5.0 to support her assertion that the two may be optimally combined to arrive at the invention of the pending claims, including an optimized yield of greater than 60%, said range including up to 70%, 80% and even 90%. However, while it is true that the temperature range disclosed in Wallace overlaps with that of the present claims at the specific value of 20° C, when one considers the reference as a whole, it becomes clear that the claimed combination is neither taught nor suggested by Wallace.

Wallace suggests that the disclosed process is performed at a pH ranging from 5.0 to 6.95, more preferably about 6.5 to 6.95, using a solution chilled to a temperature of about 2°- 20° C, preferably about 2.5°- 7.5°C (col. 2: 37-40, emphasis added). Wallace later suggests that the disclosed processes may be used to obtain a yield of “greater than 50%”, preferably “greater than 60%” of the fibronectin (col. 4: 41-42). One of skill in the art, in considering these two sections together, would readily expect that only use of the more preferred conditions (i.e., pH of 6.5 to 6.95 and temperature of 2.5°- 7.5°C) would give rise to the more preferred yield of “greater than 60%”. The skilled artisan would likewise expect that any deviation from these preferred conditions (e.g., pH of 5.3 and temperature of 20°C) would give rise to a lesser yield (i.e., less than 60%, more likely less than 50%). Accordingly, Applicants respectfully submit that the presently claimed process, including a process temperature of 20°C to 25 °C, a process pH

between 4.7 and pH 5.3, and a fibronectin yield of 70% to 99%, cannot be fairly characterized as obvious in view of the Wallace disclosure.

Furthermore, it is apparent from a comparison of Wallace's Figures 1 and 2 that only the preferred parameters (pH of 6.5 to 6.95 and temperature of 2.5°- 7.5°C) permit single step removal (Figure 1: an acid-chill precipitate process). Conversely, if one utilizes a lower pH (i.e., a pH 5.0 to 6.8, more preferably 5.8 to 6.4) and omits the chilling step, a distinct two-step procedure such as that shown in Figure 2 is required to remove fibronectin (step one: acid precipitate, step two: chill precipitate). The accompanying specification suggests that a chill precipitate such as produced by the process of Figure 2 has substantially more fibronectin-like activity than either the acid-chill precipitate of Figure 1 or the acid-precipitate of Figure 2 (col. 3, lines 28-30). This confirms Applicants' position that Wallace suggests (a) towards a two-step process and (b) away from a one-step acid-precipitate process such as that presently claimed, which together give rise to an expectation that the process as presently claimed would be less effective, providing a yield of less than the preferred 60% and more likely less than 50% -- certainly well below the 70% to 99% fibronectin recovery required by the pending claims.

On the issue of overlapping ranges, Applicants wish to remind the Examiner that a presumption of obviousness may be rebutted by showing that (a) the prior art teaches away from the claimed invention, or (b) the invention provides new and unexpected results relative to the prior art. *Iron Grip Barbell Co., Inc. v. USA Sports, Inc.*, 392 F.3d 1317, 1322, 73 USPQ2d 1225, 1228 (Fed. Cir. 2004). In this case, Applicants respectfully submit that both (a) and (b) are true. With regard to the former, as noted above, Wallace teaches away from the combination of claimed parameters, particularly the combination of a single acid-precipitate step performed at 20°C or higher, as a means for improving fibronectin recovery. With regard to the latter, Applicants have clearly demonstrated that fibronectin removal is most efficient at room temperature (e.g., 20°C), in contrast to the prior art suggestions that cold temperatures are required. See Table 2 of Applicants' specification. Applicants respectfully submit that the unexpected superior results obtained could not have been predicted by one of ordinary skill in the art, particularly in view of the teachings of Wallace that clearly suggest towards the combination acid-chill procedure, and thus serve as further indicia of non-obviousness.

Thus, Applicants respectfully submit that the invention of the pending claims cannot be fairly characterized as obvious in view of Wallace disclosure. Nevertheless, in an effort to expedite prosecution, Applicants have amended independent claim 2 to require the limitations of dependent claim 9, now cancelled. Applicants respectfully submit that the incorporation of such limitations renders moot the rejection of claims 2, 4-8, 14, and 24 as obvious over Wallace alone as well as the rejection of claims 15 and 17 as obvious over Wallace in view of BR. As for the previous rejection of claims 9-13 as obvious over Wallace in view of Newman, Applicants offer the following comments:

In order to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

In this case, the Examiner suggests that the limitations of claim 9, namely the use of plasma fraction containing NaCl or KCl at a concentration of 100 – 200 mM, are met by the Newman reference. However, Newman at column 2, lines 22-24 discloses a suspended cryoprecipitate containing 60 mM glycine and 40 mM sodium chloride at pH 7. This is clearly outside the range required by the pending claims, which set a minimum sodium chloride concentration at 100 mM. In addition, Wallace discloses solubilizing the cryoprecipitate in an aqueous medium, preferably water (col. 3: 14-15), more particularly in 10 liters of sterile water at 32°C (see Example 1). Thus, there is no disclosure in either reference to include 100 – 200 mM of sodium or potassium chloride (claim 2) or 100 to 150 mM glycine (claim 13)

Thus, in that neither Wallace nor Newman disclose or suggest the inclusion of NaCl or KCl at a concentration of 100 – 200 mM, the combination of the two cannot serve to render obvious the invention of the pending claims. As such, Applicants respectfully request reconsideration and withdrawal of the outstanding rejections under 35 U.S.C. § 103(a) in view of the amendments and remarks herein.

CONCLUSION

In view of the foregoing, Applicants respectfully submit that claims 2, 4-8, 10-15, 17, and 24 are in condition and respectfully petition for the early issuance of a Notice of Allowance confirming such.

The Office Action of September 2, 2009 set a three-month shortened statutory period for response. Further to the petition for one-month extension of time submitted herewith, response is due on or before **January 4, 2010** (January 2nd being a Saturday). Accordingly, Applicants submit that this response is timely and no additional fees, apart from those included herewith, are required. However, in the event that further fees are required to enter the instant response and/or maintain the pendency of this application, the Commissioner is authorized to charge such fees to our Deposit Account No. 50-2101.

If the Examiner has any questions or concerns regarding this communication, she is invited to contact the undersigned.

Respectfully submitted,

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